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ANIMAL MODELS IN IMPULSE NOISE RESEARCH

G. Richard Price

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The growing concern for animal rights has made it incumbent upon the scientist to justify the use of animal models in research. This report focuses on research on hearing hazard from impulse noise and develops arguments for the use of animal models based on ethical, practical, and theoretical/experimental considerations. A variety of issues require the use of animal ears in research with intense impulse noises. Two of them are especially compelling. First, because we now know that sudden and unpredictable permanent damage can occur with intense impulsive sounds, they represent a hazard to which human ears should not be exposed, especially in an experimental setting. Second, the experiments that are most likely to provide critical theoretical information are hazardous, invasive, and/or require sacrifice of the ear in their execution.

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If human ears cannot be used and animal models are the only way to acquire the critical data or to validate mathematical models, then animal models must play a central role in advancing our scientific understanding and promoting the public interest in accurate rating and control of noise hazard. The next phases of research should concentrate on the basic issues of cochlear function in response to numbers of impulses, impulses of differing intensities, mixes of impulse and continuous stimulation, as well as on the basic mechanisms of loss as a function of level.

Keywords: Blast overpressure, Deafness, Anatomical models (AW)

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CONTENTS

ANIMAL MODELS IN IMPULSE NOISE RESEARCH

INTRODUCTION

In recent years, the actions of activists for animal rights have focused attention on the use of animal models in scientific research. As a result, careful scrutiny is being given to experiments using animal subjects, a process often involving multiple reviews by committees including disinterested parties. It has always been incumbent upon the scientist to balance the use of particular experimental techniques with the need for knowledge. In the past, this decision has been essentially a private matter. However, with growing public interest in the subject and accompanying governmental/institutional involvement, the scientist needs to make public the considerations leading to the use of animal subjects in specific experimental designs (see, for example, remarks in Holden, 1987).

Given the idiosyncratic nature of individual research programs, arguments regarding the use of animals must be rather closely tailored to specific issues. Therefore, this report will attempt the dual function of outlining contemporary problems in impulse noise research and pointing out the uses to which animal models can and should be put.

BASIS FOR ANIMAL USE

Depending on one's interests, there are several different approaches to an analysis of the necessity for animal models in basic research on impulse noise. Three types of answers will be developed in this report based on (1) ethical, (2) practical, and (3) theoretical/ experimental considerations.

Ethical Considerations

The issue of impulse noise exposure is not one that can be dismissed as frivolous, irrelevant, or esoteric. Furthermore, at this early stage in the development of knowledge, where so little is known, the need for research in impulse noise is sufficiently apparent that the requirement for research can almost be taken as a premise. Nevertheless, the basis of need for this research will be examined from a variety of viewpoints.

Arguments for the institution of programs in both research and hearing conservation have been made by focusing on both the human and financial costs of noise-induced hearing loss. To illustrate the financial costs, the Veterans Administration's payments for compensation for noise-induced hearing loss will exceed $175,000,000 in 1987 alone. Far more important, but harder to quantify, is the personal suffering these 200,000+ cases of hearing loss represent.

There are also applied interests in the accurate rating and control of impulse noise exposures. In the formulation of both health hazard assessment procedures and design criteria for impulse-producing devices, accuracy of assessment is critical. Accurate assessment avoids the errors and

costs of both the under- and overestimation of the hazard from an impulse. In a military setting, both types of error bring their own penalties. Exposure limits that are excessively restrictive penalize weapon design and resulting effectiveness, thereby protecting hearing while risking life through inadequate weapon performance. On the other hand, standards that are too lax could result in hearing impairment and resulting poor job performance, to say nothing of the production of long-term handicaps.

Furthermore, given the present technologies, nonexposure to impulse noise hazard is not a realistic option for millions of persons in the armed forces around the world. Virtually all weapons that fire a projectile also produce acoustic impulses that can (and <u>do</u>) produce permanent hearing losses. And, in addition to impulse noise exposure in the armed forces, additional millions fire weapons in a recreational setting. So for whatever reasons, impulse noise exposure <u>will</u> occur and the need for knowledge of its effects is apparent.

There is considerable evidence that at high sound pressure levels, the processes that produce hearing loss change form and become essentially mechanical in character (Hamernik, Turrentine, & Roberto, 1986; Price, 1981, 1983; Spoendlin, 1976). This results in sudden, permanent changes in the ear's structure for small changes in stimulation (e.g., Borchgrevink, Woxen, & Oftedal, 1986). If this region of the ear's susceptibility is to be studied meaningfully, then it must be studied at those levels producing damage. Extrapolation upward from lower levels where the mechanisms of loss are different is not a logically valid procedure.

Further, evidence has recently been produced that even small changes in auditory threshold, if produced by intense sounds, may not fully recover (Price, 1986a). For example, in Figure 1, the threshold shift measured in the cat ear 1 to 3 hours after exposure to 50 impulses from a 105 mm howitzer is correlated with permanent threshold shift (PTS). Similar data are available for exposures to rifle or primer impulses as well (Price, 1986b). The correlation coefficients range from 0.7 to 0.8, and the slope of the regression line is a little over 0.5, indicating that a little less than half the threshold shift recovers. Furthermore, the regression line crosses the abscissa near zero, indicating that even small threshold shifts (present 1 or 2 hours after exposure) may have a permanent component. This finding is in contrast to the conventional wisdom (based on lower-level exposures) that so long as a shift is below 40 dB or so, it will recover.

If the potential exists for permanent change in the ear's structure as a result of an exposure in an experiment, then the use of human subjects in such studies is not ethically acceptable. This is one of the reasons for the scarcity of data on human ears and the limitation of experimental observations with human subjects to the monitoring of thresholds in protected ears when firing exercises or other tests are run (e.g., Hodge, Price, Dukes, & Murff, 1979; Pfander, Bongartz, Brinkmann, & Kietz, 1980).

This reluctance to use humans is especially understandable when there are alternatives to the risks associated with using human ears. Although there are considerable differences in the external ears of various mammals, the inner ears (the primary damage site) are essentially similar in structure (Dancer, 1981) and provide an alternate approach to arrive at the accurate, theoretically based knowledge needed. Once the knowledge base is developed through experiments with experimental animals, the results can then be extrapolated to the human and the application verified.

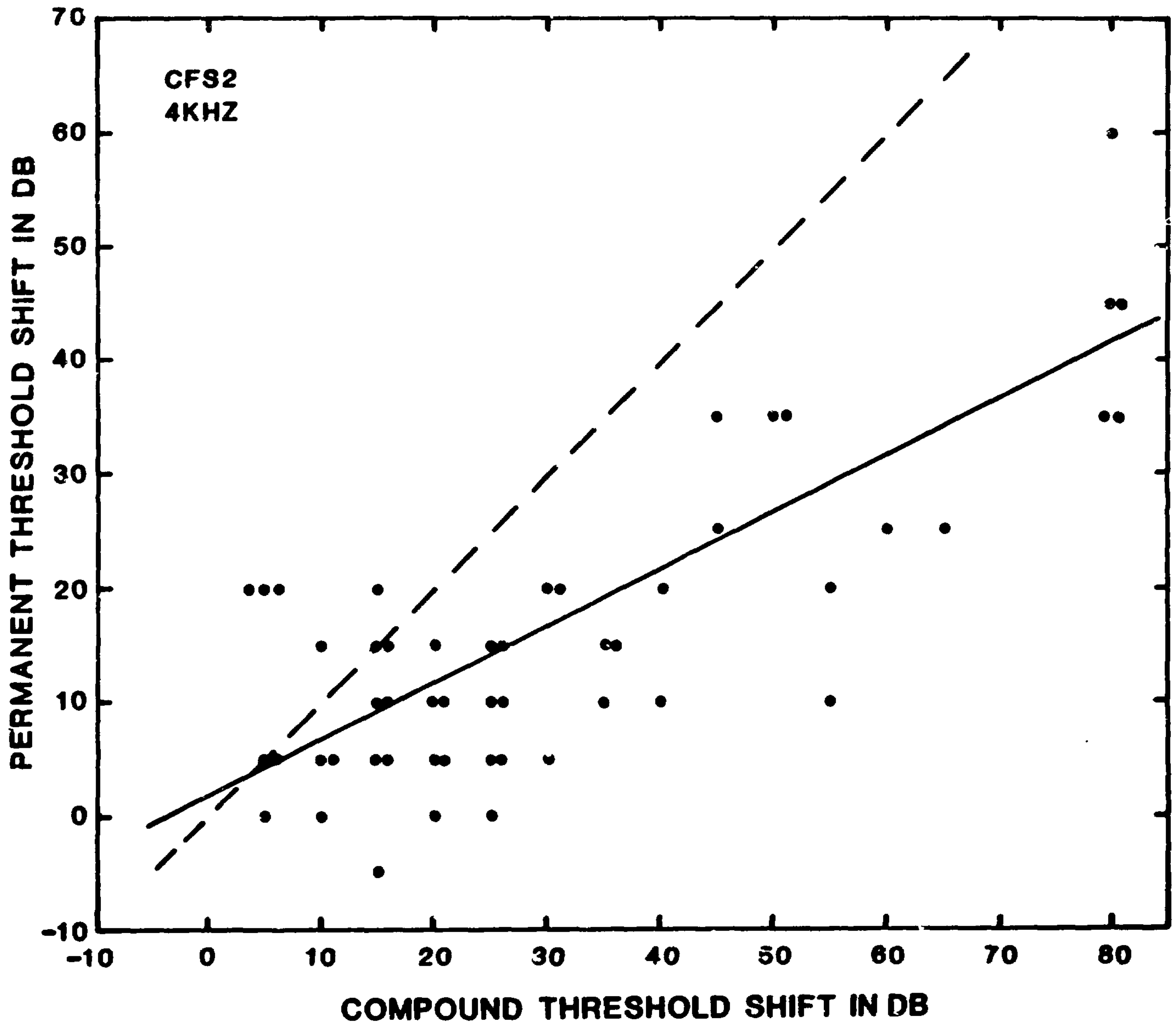

Figure 1. Permanent threshold shift (PTS) at 4.0 kHz measured in cat ears exposed to 50 impulses from a 105 mm howitzer as a function of the threshold shift 1 to 3 hours postexposure (Price, 1986a).

There are also ethical constraints on the type of measures that can be obtained from human subjects. Those using invasive and/or risky techniques can rarely be justified for use with humans. Experiments using histological data or measures of intracochlear electrical potentials, pressures, or displacements are among the most interesting that can be performed; but none of these measures can be used with human subjects (except postmortem). The need for experiments using such measures will be discussed later in this report.

Practical Considerations

Even if a particular experiment might be performed equally well with human or animal ears, there are situations in which the animal offers certain practical advantages. The cost of most commonly used species is relatively low, although there are expenses associated with housing and maintaining them once they are procured. These requirements do add measurably to the costs of doing research with animals. However, from the experimenter's standpoint, the animal subjects are extremely convenient. They can wait extended periods until the conditions are correct for their use, they can be maintained in experimental settings for protracted periods, their activities can be monitored to ensure that the effects seen are due only to the experimental exposure and not to exposure associated with leisure time activities or with conditions (noise exposure, disease, drug use, etc.) that preceded the experiment. The animal can be reared from conception within a colony so that its entire life history is known. The result is that with animal data there can be fewer uncontrolled variables, the data can be cleaner, and fewer animals/experiments may be needed to achieve a given level of certainty.

Another type of practical consideration is that much of the work already done over the years in physiological acoustics has been done with animal subjects. Therefore, there is a great deal of data on various aspects of the functioning of the ear already available, for example, transfer functions of the middle ear, ear drum displacement patterns, tuning of the cochlea, etc. Experimental programs using animal ears can therefore build on a wealth of existing data.

Theoretical and Experimental Considerations

The most important justification for the use of animal subjects is that the crucial voids in knowledge can be filled only through the type of experiments that can be done with animal ears. At this point in the development of our knowledge, there are four important issues that can be approached best with animals. First, nonlinearities in the middle ear have a major influence on the stimulation actually transmitted to the inner ear and thus may explain the peculiarities in the ear's susceptibility. Second, the fundamental mechanisms of loss within the cochlea are essentially unknown and need to be elucidated. Third, there is ample evidence that what has just happened to an ear affects its susceptibility to subsequent stimulation; yet the interactions are virtually unexplored. Lastly, mathematical models of the ear's response provide the hope of insight that will allow us to understand the fundamental mechanisms and deal with the impulse noise problem; however, the models' predictions need to be tested. For this work, the use of animal ears is mandatory. Each of these four areas will be discussed in turn.

1. The effect of the middle ear mechanisms on susceptibility

Calculations with a mathematical model of the ear have focused attention on the possibility that conductive properties of the middle ear play a profound role in determining the ear's susceptibility to intense sounds (Kalb & Price, 1987; Price & Kalb, 1986). Based on the anatomical structure and measurements in the cat ear (Guinan & Peake, 1967), it has been argued that the annular ligament of the stapes is in a position to control transmission into the cochlea by limiting stapes displacement to about 40 microns or so, peak to peak. This effect is seen in Figure 2, which shows the measurements of Guinan and Peake (1967) (data points) and the model fitted to the data (solid line). In essence, once the amplitude limitation begins to have an effect, increases in sound pressure are not reflected in proportionate increases in cochlear stimulation. The effect of such a limitation on the energy transmitted into the cochlea can be immense, as seen in Figure 3. The curves were calculated by driving the model with Friedlander waveforms with one of two A-durations (0.35 or 2.0 msec, typical of a rifle and a howitzer respectively) and calculating the energy present in 1/3-octave bands at the input to the cochlea as the peak pressure was increased through a range commonly experienced around weapons. The figure demonstrates a number of points. If we look first at the rifle-like impulse (0.35 msec A-duration, dashed lines), we see that as the pressure rises in 10-dB steps from 140 to 160 dB, the energy in any band also rises. But generally this occurs in increasingly smaller steps, as one might expect from the increase in clipping at higher pressures. In the midrange, which is where damage tends to be greatest for almost any impulse, the compression tends to be greatest. For example, at 5.0 kHz, the energy grew only 3 dB for an increase in pressure from 150 to 160 dB. One point of exception is at 8.0 kHz where the energy increases about 12 dB (140- to 150-dB step), presumably because of harmonics introduced by the clipping.

Because of its onset at lower pressures, the clipping effect is even more dramatic for the low-frequency Friedlander. The energy was calculated in this case for peak pressures of 140, 150, and 180 dB. As pressure rises, the same nonlinear growth is seen. It is noteworthy that whereas both the 140-dB waveforms had essentially the same energy in the midrange, because of the clipping, even the 180-dB "howitzer" impulse had less energy there than did the 160-dB "rifle."

If this amplitude limitation does indeed operate for weapons impulses, it is crucial that it be verified and its mechanics understood. This effect is at present the only explanation for the observations that all damage risk criteria (DRCs) in use overrate the hazard from low-frequency impulses (large weapons) (Price, 1986b). Experiments directly testing the hypothesized limitation of displacement must be performed on animal ears because measures are invasive. In fact, Franke and Dancer (1978) did perform intracochlear pressure measurements in the guinea pig and they showed a nonlinear growth of pressure at high levels, especially for low-frequency stimuli. This work needs to be expanded to include a greater range of parameters and with additional species to document the effect fully so that it might be understood and even exploited to reduce hazard.

Additionally, the transfer function of the middle ear also has the effect of band-pass, filtering the energy it transmits. This effect is responsible for much of the detail in the ear's response to intense stimulation (Price, 1981).

2. Intracochlear mechanism(s) responsible for loss

At the present time, the best hypothesis we have regarding the intracochlear mechanisms responsible for hearing loss is that at high levels the processes are fundamentally mechanical. A few corollaries to this hypothesis have been advanced (Broch, 1979; Price, 1983). However, the cochlea is not a simple structure, the properties of its membranes are only poorly

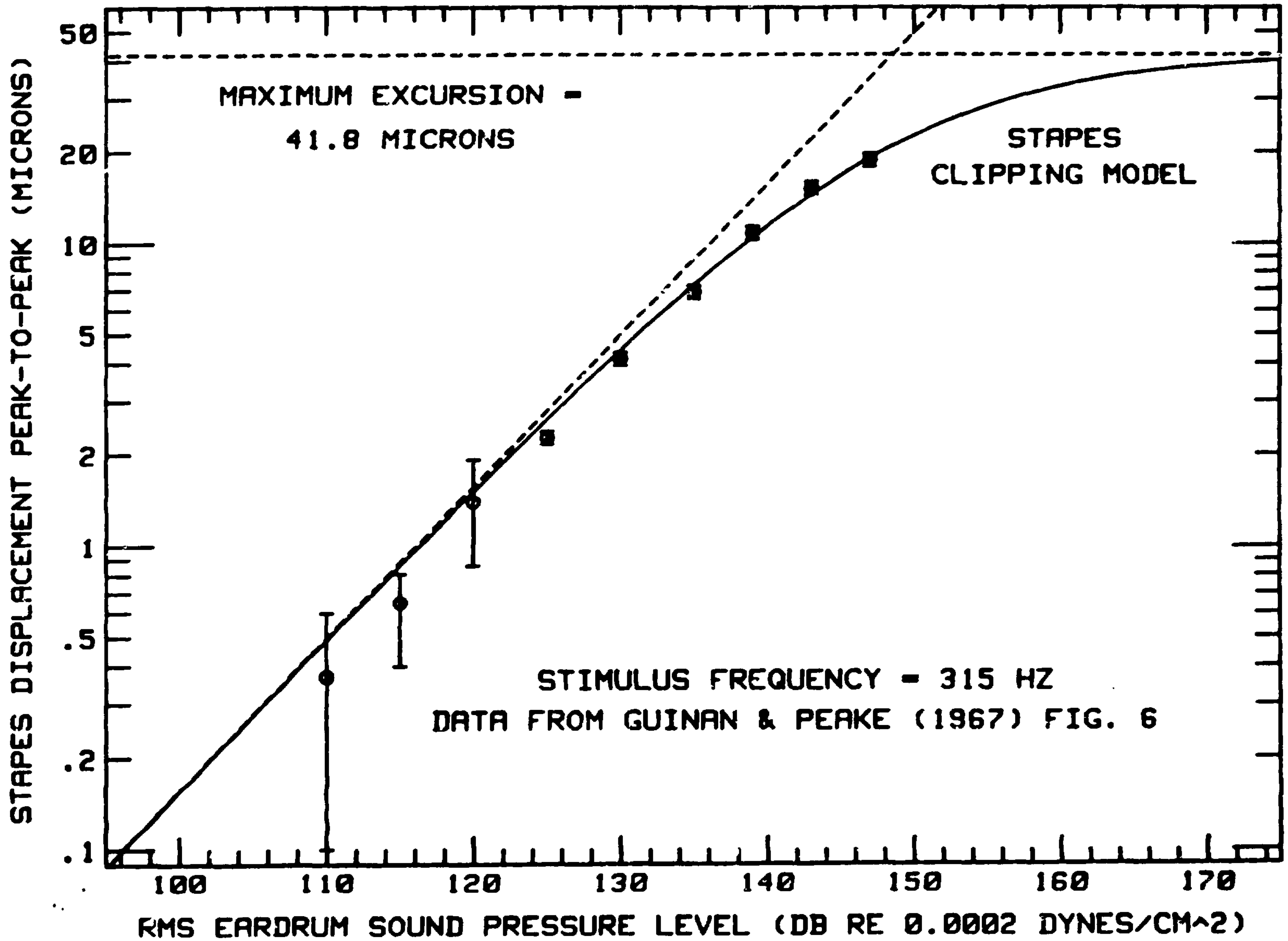

Figure 2. Stapes displacement as a function of sound pressure level (data points from Guinan & Peake, 1987) fitted by a mathematical model (dotted line from Kalb & Price, 1987).

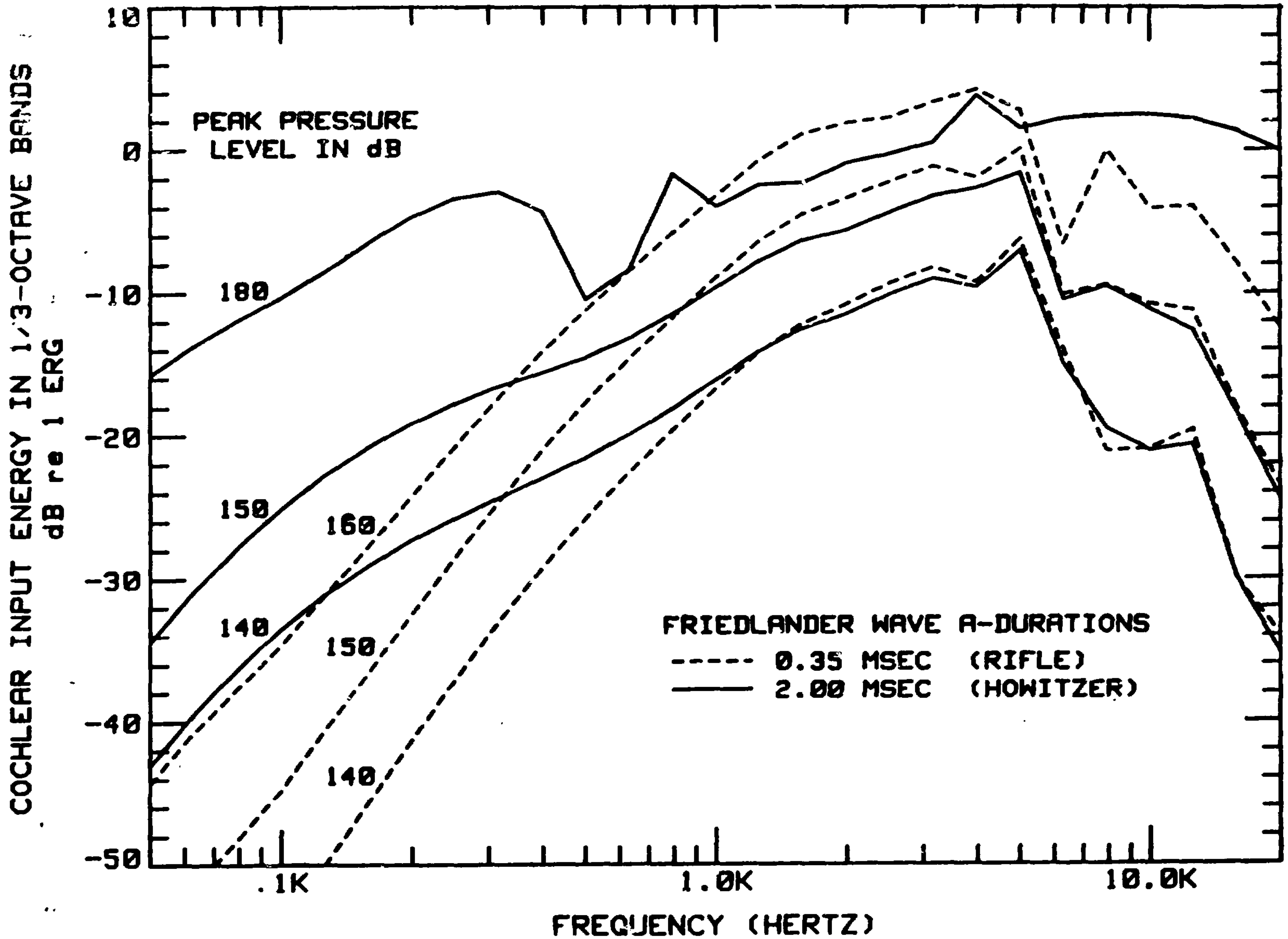

Figure 3. Calculated energy in 1/3-octave bands transmitted to the cochlea by Friedlander waveforms with A-durations of 0.35 and 2.0 msec, characteristic of rifle and howitzer impulses, respectively, at peak sound pressures from 140 to 180 dB. Calculation based on model by Kalb and Price (1987).

known, and almost nothing is known regarding its fatigue response to high-amplitude cyclic distortions. Because tissue changes within the organ of Corti are primarily responsible for the hearing loss, it follows that knowledge of the mechanisms involved is essential to an adequate understanding of the ear's susceptibility.

If we are ever to be able to apply the basic research to specific problems, knowledge of the basic mechanism responsible for loss will play a critical role. For example, if the processes are fundamentally mechanical (the ear is being torn up), exposure at such a level will have to be severely limited or avoided. On the other hand, if the processes are fatigue-like (the ear is being tired out), it is reasonable to consider ways of accumulating exposures, mixes of high- and low-level exposures, etc.

Some preliminary results from modeling intracochlear displacements have been encouraging in that they have shown the correct correspondence between predicted displacements in response to rifle and cannon impulses and the ear's actual susceptibility, something no other measure has so far been able to do (Kalb & Price, 1987) (Figure 4). In Figure 4, we see the predicted basilar membrane displacements at the most susceptible site for both howitzer and rifle impulses of increasing intensity. For the displacements to be equal, the howitzer's peak pressure must be about 10 dB higher than the rifle, which is the experimentally determined relationship for equal hazard for these same impulses (Price, 1986b). This is a very encouraging result; however, the work is only beginning and considerably more will have to be done. It is likely that focusing attention at the level of intracochlear events will provide important keys to solving the impulse noise problem. For a variety of ethical and practical reasons, verification of the predictions of the model will depend almost exclusively on data from experiments with animal ears.

3. Interactions between exposures

The third arena where experiments with animal ears will be essential is that of exploring and quantifying the interactions between different exposures. In the previous section we were concerned with understanding the fundamental mechanism(s) of loss associated with a single exposure to intense stimulation; but in many situations the ear will be be exposed to mixes of more and less intense stimulation, continuous and impulsive sounds, for varying periods of time, with differing temporal patterns, etc. There is ample evidence that there is no simple relationship between energy and hearing loss. The correlation between immission and hearing loss was studied by Taylor and Pelmear (1976) for exposure to drop-forging noise. The correlation was very poor, with almost none of the variance being explained. It is clear that even for these relatively restricted exposures, the ear is not a simple energy integrator; rather it is a living system complete with its inherent homeostatic mechanisms. At present, the following four relationships need to be explored: (1) exposures to various numbers of impulses at any given level, (2) exposures to various levels of impulse, (3) combinations of high- and lower-level exposure, and (4) the temporal pattern of exposure.

(a) Number of impulses. What allowance should be made for growth of hazard from different numbers of impulses? There are almost no data that bear on this point, even though the existing DRCs make allowances for the number of rounds. Data from Kraak (1981) and Hamernik, Patterson, and Salvi (1987) do suggest a correlation with energy.

(b) Different levels of impulse. How does hazard grow with intensity? Again, there are few data bearing on this point. The summation of energy is one possibility; however, if the middle ear is nonlinear in this intensity region, it is hard to see how any simple relationship could hold.

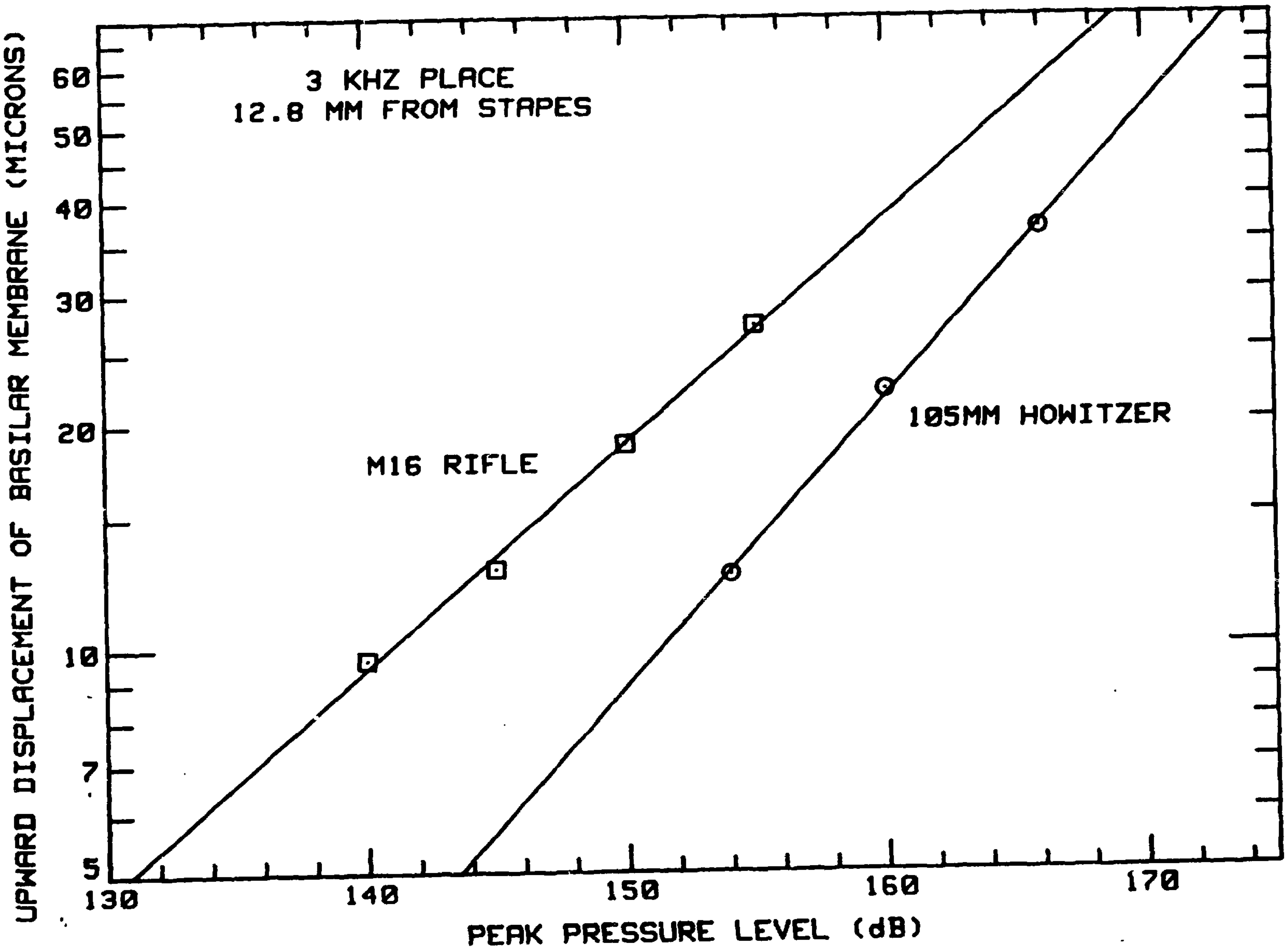

Figure 4. Calculated peak upward basilar membrane displacement in response to actual rifle and howitzer impulses of various intensities (Kalb & Price, 1987).

(c) High- and lower-level exposures. How should exposures be evaluated when they consist (as they almost all will) of impulses with different peak pressures? Or for that matter, how do exposures to intense impulses interact with lower-level exposures, as when men ride in armored vehicles and then shoot? There is some evidence from Hamernik, Henderson, Crossley, and Salvi (1974) that there may be a synergism, that is, the ear exposed to a lower-intensity sound may be much more susceptible to an intense impulse.

(d) Timing between exposures. There is considerable evidence that the time between exposures can have a large effect on hazard, even when the total energy in the sound field is kept constant and the peak pressure is kept constant. The middle ear muscle reflex can attenuate impulses if they are close enough together (thereby reducing the hazard) (Ward, 1962); or there is evidence that the hazard may even be dramatically increased, due to intracochlear factors, if the spacing is too small (Perkins, Hamernik, & Henderson, 1975; Price, 1974, 1976). Given the large effects produced by the timing of the impulses, it is essential that the temporal dynamics of the ear under the stress from intense impulses be studied.

Again, the only practical way to explore the interactions between exposures is through the use of animal ears that can be exposed at realistic levels and in which the effects can be measured by a range of techniques.

4. Validation of predictions from modeling

The final area where animal experiments may be particularly valuable is in validating models of the ear. As indicated earlier, no traditional weighting of an acoustic measurement is an adequate descriptor of hazard; therefore, it appears that models will have an important role to play in establishing hazard from impulsive sounds. And we have shown that at least one model does rank a limited set of hazards correctly. However, models are notoriously good at reproducing existing data (on which they are based) and need to be validated with new measures of all types. Because of the hazard to the ear and the invasiveness of the measures needed for these validation studies, experiments with animal ears will be essential.

In addition, the use of animal ears has the potential for "manipulation" of the ear itself. By selection of several species with a particular configuration of their auditory systems, it is possible to test the relative roles played by different physical parameters, such as the resonant frequencies, compliances of various structures, etc.

Real hope exists for mathematical modeling. With improvements in the technology of microprocessors and with a better understanding of the mechanisms of hazard in the inner ear as reflected in improved models of the ear, easily measured and accurate ratings of hazard will ultimately be possible.

CONCLUSION

It is apparent that a variety of considerations require the use of animal ears in research with intense impulse noises. Two of them are especially compelling. First, because we now know that sudden and unpredictable permanent damage can occur, intense impulsive sounds represent a hazard to which human ears should not be exposed, especially in an experimental setting. Second, the experiments that are most likely to provide the critical information are hazardous, invasive,

and/or require sacrifice of the ear in their execution. If human ears cannot be used and animal models are the only way to acquire the critical data or to validate mathematical models, then it is apparent that if our scientific understanding is to go forward, animal models will play a central role.

From the standpoint of the issues on which research on impulse noise needs to be concentrated, we see that the basic issues of cochlear function in response to numbers of impulses, impulses of differing intensities, mixes of impulse and continuous stimulation, as well as research on the basic mechanisms of loss all remain to be addressed.

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